

Fig. 9)

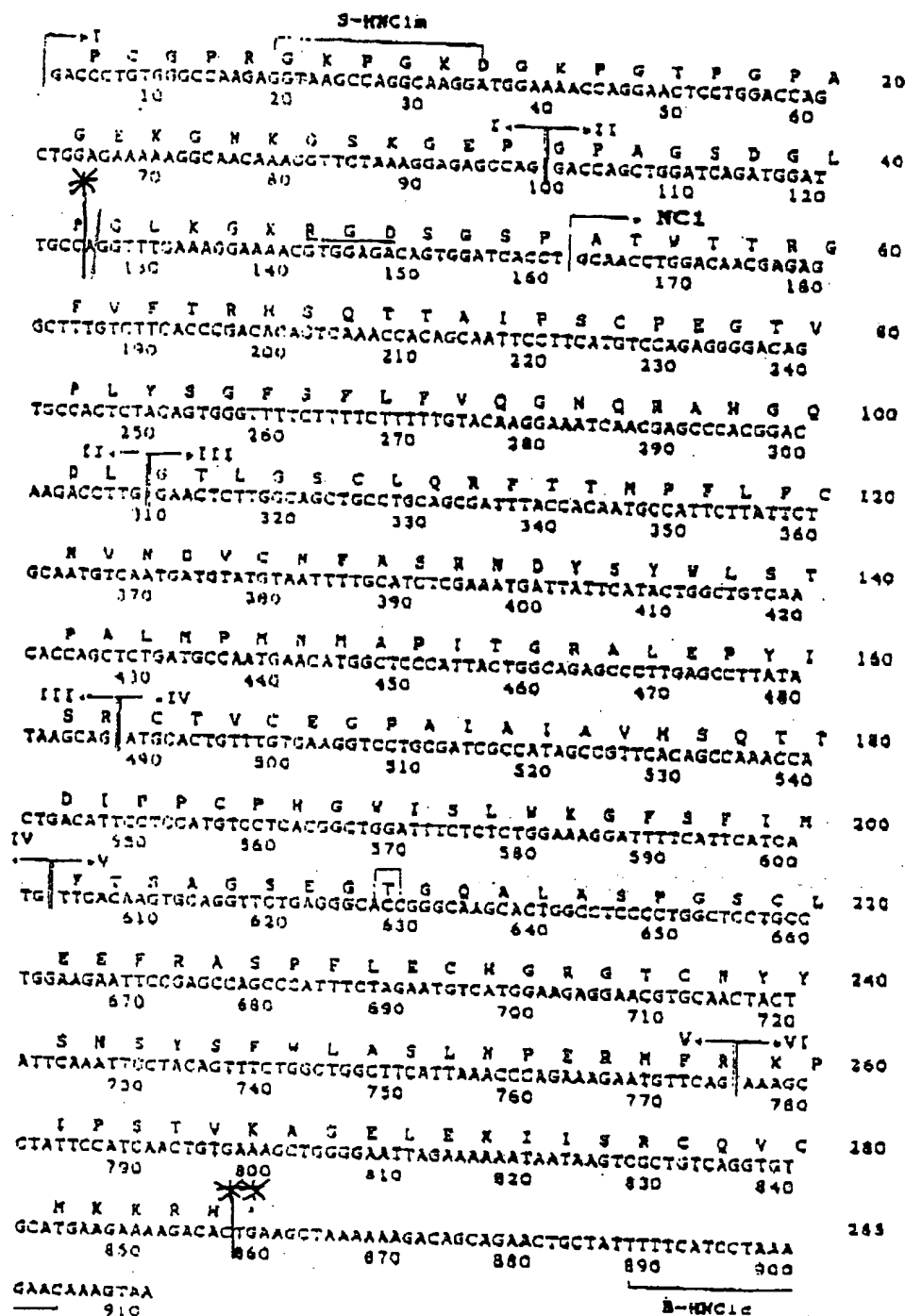


FIG. 2. Nucleotide and derived amino acid sequence of HGA3.3 exons. Bent arrows indicate the 5'- and 3'-borders of each exon and the beginning of the NC1 domain. The RGD sequence is underlined. The boxed amino acid is different from that previously reported (11). Positions of the oligonucleotides S-HNC1m and B-HNC1c used for PCR amplification of a human  $\alpha 3$ (IV) cDNA are indicated. Amino Acids 1-67 have not been previously reported (11).

EXHIBIT

A

tabbles

tled3

ay, June 7, 1998 12:44 PM

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      10      20      30      40
*      *      *      *
GLK GKR GDS GSP ATW TTR GFV FTR HSQ TTA IPS CPE GTV PLY SGF
____1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV____>

      50      60      70      80      90
*      *      *      *      *
SFL FVQ GNQ RAH GQD LGT LGS CLQ RFT TMP FLF CNV NDV CNF ASR
____1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV____>

      100     110     120     130
*      *      *      *      *
NDY SYW LST PAL MPM NMA PIT GRA LEP YIS RCT VCE GPA IAI AVH
____1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV____>

      140     150     160     170     180
*      *      *      *      *
SQT TDI PPC PHG WIS LWK GFS FIM FTS AGS EGT GQA LAS PGS CLE
____1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV____>

      190     200     210     220
*      *      *      *      *
EFR ASP FLE CHG RGT CNY YSN SYS FWL ASL NPE RMF RKP IPS TVK
____1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV____>

      230     240
*      *      *
AGE LEK IIS RCQ VCM KKR H
____1427 TO 1670 OF FU____>

```

Fig. 10

# FIG. 18A

pET22b(+) forward primer:

5'-CGGGAT CCA GGT TTG AAA GGA AAA CGT-3' (SEQ ID NO:11)

pET22b(+) reverse primer:

5'-CCCAAGCTT TCA GTG TCT TTT CTT CAT-3' (SEQ ID NO:12)

5	10	15	20	25	30	35	40	45
<del>cca</del> ggt ttg aaa gga aaa cgt	gga gac agt gga tca cct gca acc							
50	55	60	65	70	75	80	85	90
tgg aca acg aga ggc ttt gtc ttc acc	cga cac agt caa acc aca							
95	100	105	110	115	120	125	130	135
gca att cct tca tgt cca gag ggg aca	gtg cca ctc tac agt ggg							
140	145	150	155	160	165	170	175	180
ttt tct ttt ctt ttt gta caa gga aat	caa cga gcc cac gga caa							
185	190	195	200	205	210	215	220	225
gac ctt gga act ctt ggc agc tgc ctg	cag cga ttt acc aca atg							
230	235	240	245	250	255	260	265	270
cca ttc tta ttc tgc aat gtc aat gat	gta tgt aat ttt gca tct							
275	280	285	290	295	300	305	310	315
cga aat gat tat tca tac tgg ctg tca	aca cca gct ctg atg cca							
320	325	330	335	340	345	350	355	360
atg aac atg gct ccc att act ggc aga	gcc ctt gag cct tat ata							
365	370	375	380	385	390	395	400	405
agc aga tgc act gtt tgt gaa ggt cct	gcg atc gcc ata gcc gtt							
410	415	420	425	430	435	440	445	450
cac agc caa acc act gac att cct cca	tgt cct cac ggc tgg att							
455	460	465	470	475	480	485	490	495
tct ctc tgg aaa gga ttt tca ttc atc	atg ttc aca agt gca ggt							
500	505	510	515	520	525	530	535	540
tct gag ggc acc ggg caa gca ctg gcc	tcc cct ggc tcc tgc ctg							
545	550	555	560	565	570	575	580	585
gaa gaa ttc cga gcc agc cca ttt cta	gaa tgt cat gga aga gga							
590	595	600	605	610	615	620	625	630
acg tgc aac tac tat tca aat tcc tac	agt ttc tgg ctg gct tca							
635	640	645	650	655	660	665	670	675
tta aac cca gaa aga atg ttc aga aag	cct att cca tca act gtg							
680	685	690	695	700	705	710	715	720
aaa gct ggg gaa tta gaa aaa ata ata	agt cgc tgt cag gtg tgc							
725	730	735						
atg aag aaa aga cac tga								

(SEQ ID NO:9)

pET22b- $\alpha$ 3(IV) NC1 = nucleotides ~~4~~ through ~~735~~ 732

Tumstatin 333 = nucleotides ~~4~~ through ~~375~~ 372

Tumstatin 334 - nucleotide ~~376~~ through ~~735~~ 732

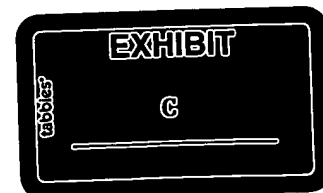
373



# FIG. 18B

\*  
5 10 15 20 25 30 35 40 45  
XGL KGK RGD SGS PAT WTT RGF VFT RHS QTT AIP SCP EGT VPL YSG  
50 55 60 65 70 75 80 85 90  
FSF LFV QGN QRA HGQ DLG TLG SCL QRF TTM PFL FCN VND VCN FAS  
95 100 105 110 115 120 125 130 135  
RND YSY WLS TPA LMP MNM API TGR ALE PYI SRC TVC EGP AIA IAV  
140 145 150 155 160 165 170 175 180  
HSQ TTD IPP CPH GWI SLW KGF SFI MFT SAG SEG TGQ ALA SPG SCL  
185 190 195 200 205 210 215 220 225  
EEF RAS PFL ECH GRG TCN YYS NSY SFW LAS LNP ERM FRK PIP STV  
230 235 240 245-244  
KAG ELE KII SRC QVC MKK RH (SEQ ID NO:10)

pET22b  $\alpha$ 3(IV) NC1 = residues 1 through 245-244  
Tumstatin 333 = residues 1 through 125-124  
Tumstatin 334 = residues 126 through 245-244  
125



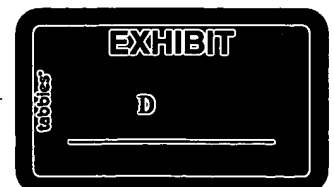
## FIG. 42

T1 GP-A  
PGLKGKRGDSGSPATWTTTRGFVFTRHSQTTAIPSCPEGTVPLY

T2 T3  
SGFSFLFVQGNQRAHGQDLGTLGSC LQRFTTMPFLFCNVNDVC

T3 T4 T5  
NFASRNDYSYWLSTPALMPMNMAPITGRALEPYISRCTVCEGP

T6 GP-B  
AIAIAVHSQTTDIPPCPHGWISLWKGFSFIMFTSAGSEG TGQA  
LASPGSCLEEFRA SPFLECHGRGTCNYYSNSYSFWLASLNPER  
MFRKPI PSTVKAGELEKIISRCQVCMKKRH



## SEQUENCE LISTING

&lt;110&gt; Raghuram Kalluri

<120> ANTI-ANGIOGENIC PROTEINS AND FRAGMENTS  
AND METHODS OF USE THEREOF

&lt;130&gt; 1440.1027-016

{ <140> US 10/032,221  
 { <141> 2001-12-21

&lt;150&gt; PCT/US01/00565

&lt;151&gt; 2001-01-08

&lt;150&gt; US 09/543,371

&lt;151&gt; 2000-04-04

&lt;150&gt; US 09/335,224

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&lt;151&gt; 1999-03-25

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&lt;150&gt; US 09/625,191

&lt;151&gt; 2000-07-21

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&lt;212&gt; DNA

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&lt;222&gt; (1)...(687)

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 1 5 10 15

48

gac cca cag tgt cct tct ggg acc aaa att ctt tac cac ggg tac tct  
 Asp Pro Gln Cys Pro Ser Gly Thr Lys Ile Leu Tyr His Gly Tyr Ser  
 20 25 30

96

ttg ctc tac gtg caa ggc aat gaa cgg gcc cat gga cag gac ttg ggc  
 Leu Leu Tyr Val Gln Gly Asn Glu Arg Ala His Gly Gln Asp Leu Gly  
 35 40 45

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EXHIBIT

E

tabbles

2/21

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Thr Ala Gly Ser Cys Leu Arg Lys Phe Ser Thr Met Pro Phe Leu Phe	
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tgc aat att aac aac gtg tgc aac ttt gca tca cga aat gac tac tcg	240
Cys Asn Ile Asn Asn Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser	
65 70 75 80	
tac tgg ctg tcc acc cct gag ccc atg ccc atg tca atg gca ccc atc	288
Tyr Trp Leu Ser Thr Pro Glu Pro Met Pro Met Ser Met Ala Pro Ile	
85 90 95	
acg ggg gaa aac ata aga cca ttt att agt agg tgt gct gtg tgt gag	336
Thr Gly Glu Asn Ile Arg Pro Phe Ile Ser Arg Cys Ala Val Cys Glu	
100 105 110	
gcg cct gcc atg gtg atg gcc gtg cac agc cag acc att cag atc cca	384
Ala Pro Ala Met Val Met Ala Val His Ser Gln Thr Ile Gln Ile Pro	
115 120 125	
ccg tgc ccc agc ggg tgg tcc tcg ctg tgg atc ggc tac tct ttt gtg	432
Pro Cys Pro Ser Gly Trp Ser Ser Leu Trp Ile Gly Tyr Ser Phe Val	
130 135 140	
atg cac acc agc gct ggt gca gaa ggc tct ggc caa gcc ctg gcg tcc	480
Met His Thr Ser Ala Gly Ala Glu Gly Ser Gly Gln Ala Leu Ala Ser	
145 150 155 160	
ccc ggc tcc tgc ctg gag gag ttt aga agt gcg cca ttc atc gag tgt	528
Pro Gly Ser Cys Leu Glu Glu Phe Arg Ser Ala Pro Phe Ile Glu Cys	
165 170 175	
cac ggc cgt ggg acc tgc aat tac tac gca aac gct tac agc ttt tgg	576
His Gly Arg Gly Thr Cys Asn Tyr Tyr Ala Asn Ala Tyr Ser Phe Trp	
180 185 190	
ctc gcc acc ata gag agg agc gag atg ttc aag aag cct acg ccg tcc	624
Leu Ala Thr Ile Glu Arg Ser Glu Met Phe Lys Lys Pro Thr Pro Ser	
195 200 205	
acc ttg aag gca ggg gag ctg cgc acg cac gtc agc cgc tgc caa gtc	672
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Asp Pro Gln Cys Pro Ser Gly Thr Lys Ile Leu Tyr His Gly Tyr Ser	
20 25 30	

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Leu Leu Tyr Val Gln Gly Asn Glu Arg Ala His Gly Gln Asp Leu Gly
   35                               40                               45
Thr Ala Gly Ser Cys Leu Arg Lys Phe Ser Thr Met Pro Phe Leu Phe
   50                               55                               60
Cys Asn Ile Asn Asn Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser
   65                               70                               75                               80
Tyr Trp Leu Ser Thr Pro Glu Pro Met Pro Met Ser Met Ala Pro Ile
   85                               90                               95
Thr Gly Glu Asn Ile Arg Pro Phe Ile Ser Arg Cys Ala Val Cys Glu
  100                               105                               110
Ala Pro Ala Met Val Met Ala Val His Ser Gln Thr Ile Gln Ile Pro
  115                               120                               125
Pro Cys Pro Ser Gly Trp Ser Ser Leu Trp Ile Gly Tyr Ser Phe Val
  130                               135                               140
Met His Thr Ser Ala Gly Ala Glu Gly Ser Gly Gln Ala Leu Ala Ser
  145                               150                               155                               160
Pro Gly Ser Cys Leu Glu Glu Phe Arg Ser Ala Pro Phe Ile Glu Cys
  165                               170                               175
His Gly Arg Gly Thr Cys Asn Tyr Tyr Ala Asn Ala Tyr Ser Phe Trp
  180                               185                               190
Leu Ala Thr Ile Glu Arg Ser Glu Met Phe Lys Lys Pro Thr Pro Ser
  195                               200                               205
Thr Leu Lys Ala Gly Glu Leu Arg Thr His Val Ser Arg Cys Gln Val
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Cys Met Arg Arg Thr

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<213> Homo sapiens

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ccc atg tgc ccg gtg ggc atg aac aaa ctc tgg agt gga tac agc ctg 96  
 Pro Met Cys Pro Val Gly Met Asn Lys Leu Trp Ser Gly Tyr Ser Leu  
 20 25 30

ctg tac ttc gag ggc cag gag aag gcg cac aac cag gac ctg ggg ctg 144  
 Leu Tyr Phe Glu Gly Gln Glu Lys Ala His Asn Gln Asp Leu Gly Leu  
 35 40 45

gcg ggc tcc tgc ctg gcg cgg ttc agc acc atg ccc ttc ctg tac tgc 192  
 Ala Gly Ser Cys Leu Ala Arg Phe Ser Thr Met Pro Phe Leu Tyr Cys  
 50 55 60

aac cct ggt gat gtc tgc tac tat gcc agc cgg aac gac aag tcc tac 240  
 Asn Pro Gly Asp Val Cys Tyr Tyr Ala Ser Arg Asn Asp Lys Ser Tyr  
 65 70 75 80

tgg ctc tct acc act gcg ccg ctg ccc atg atg ccc gtg gcc gag gac 288  
 Trp Leu Ser Thr Thr Ala Pro Leu Pro Met Met Pro Val Ala Glu Asp  
 85 90 95

gag atc aag ccc tac atc agc cgc tgt tct gtg tgt gag gcc ccg gcc 336  
 Glu Ile Lys Pro Tyr Ile Ser Arg Cys Ser Val Cys Glu Ala Pro Ala  
 100 105 110

atc gcc atc gcg gtc cac agt cag gat gtc tcc atc cca cac tgc cca 384  
 Ile Ala Ile Ala Val His Ser Gln Asp Val Ser Ile Pro His Cys Pro  
 115 120 125

gct ggg tgg cgg agt ttg tgg atc gga tat tcc ttc ctc atg cac acg 432  
 Ala Gly Trp Arg Ser Leu Trp Ile Gly Tyr Ser Phe Leu Met His Thr  
 130 135 140

gcg gcg gga gac gaa ggc ggt ggc caa tca ctg gtg tca ccg ggc agc 480  
 Ala Ala Gly Asp Glu Gly Gly Gly Gln Ser Leu Val Ser Pro Gly Ser  
 145 150 155 160

tgt cta gag gac ttc cgc gcc aca cca ttc atc gaa tgc aat gga ggc 528  
 Cys Leu Glu Asp Phe Arg Ala Thr Pro Phe Ile Glu Cys Asn Gly Gly  
 165 170 175

cgc ggc acc tgc cac tac tac gcc aac aag tac agc ttc tgg ctg acc 576  
 Arg Gly Thr Cys His Tyr Tyr Ala Asn Lys Tyr Ser Phe Trp Leu Thr  
 180 185 190

acc att ccc gag cag agc ttc cag ggc tcg ccc tcc gcc gac acg ctc 624  
 Thr Ile Pro Glu Gln Ser Phe Gln Gly Ser Pro Ser Ala Asp Thr Leu  
 195 200 205

aag gcc ggc ctc atc cgc aca cac atc agc cgc tgc cag gtg tgc atg 672  
 Lys Ala Gly Leu Ile Arg Thr His Ile Ser Arg Cys Gln Val Cys Met  
 210 215 220

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 Lys Asn Leu

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 Leu Tyr Phe Glu Gly Gln Glu Lys Ala His Asn Gln Asp Leu Gly Leu  
 35 40 45  
 Ala Gly Ser Cys Leu Ala Arg Phe Ser Thr Met Pro Phe Leu Tyr Cys  
 50 55 60  
 Asn Pro Gly Asp Val Cys Tyr Tyr Ala Ser Arg Asn Asp Lys Ser Tyr  
 65 70 75 80  
 Trp Leu Ser Thr Thr Ala Pro Leu Pro Met Met Pro Val Ala Glu Asp  
 85 90 95  
 Glu Ile Lys Pro Tyr Ile Ser Arg Cys Ser Val Cys Glu Ala Pro Ala  
 100 105 110  
 Ile Ala Ile Ala Val His Ser Gln Asp Val Ser Ile Pro His Cys Pro  
 115 120 125  
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 130 135 140  
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 145 150 155 160  
 Cys Leu Glu Asp Phe Arg Ala Thr Pro Phe Ile Glu Cys Asn Gly Gly  
 165 170 175  
 Arg Gly Thr Cys His Tyr Tyr Ala Asn Lys Tyr Ser Phe Trp Leu Thr  
 180 185 190  
 Thr Ile Pro Glu Gln Ser Phe Gln Gly Ser Pro Ser Ala Asp Thr Leu  
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 Canstatin

6/21

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~~Pro~~ Gly Leu Lys Gly Lys Arg Gly Asp Ser Gly Ser Pro Ala Thr Trp  
1 5 10 15

aca acg aga ggc ttt gtc ttc acc cga cac agt caa acc aca gca att 96  
Thr Thr Arg Gly Phe Val Phe Thr Arg His Ser Gln Thr Thr Ala Ile  
20 25 30

cct tca tgt cca gag ggg aca gtg cca ctc tac agt ggg ttt tct ttt 144  
Pro Ser Cys Pro Glu Gly Thr Val Pro Leu Tyr Ser Gly Phe Ser Phe  
35 40 45

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Leu Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln Asp Leu Gly Thr  
50 55 60

ctt ggc agc tgc ctg cag cga ttt acc aca atg cca ttc tta ttc tgc 240  
Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys  
65 70 75 80

aat gtc aat gat gta tgt aat ttt gca tct cga aat gat tat tca tac 288  
Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr  
85 90 95

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Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr  
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Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr Val Cys Glu Gly  
115 120 125

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Pro Ala Ile Ala Ile Ala Val His Ser Gln Thr Thr Asp Ile Pro Pro  
130 135 140

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Cys Pro His Gly Trp Ile Ser Leu Trp Lys Gly Phe Ser Phe Ile Met  
145 150 155 160

ttc aca agt gca ggt tct gag ggc acc ggg caa gca ctg gcc tcc cct 528  
Phe Thr Ser Ala Gly Ser Glu Gly Thr Gly Gln Ala Leu Ala Ser Pro  
165 170 175

ggc tcc tgc ctg gaa gaa ttc cga gcc agc cca ttt cta gaa tgt cat 576  
Gly Ser Cys Leu Glu Glu Phe Arg Ala Ser Pro Phe Leu Glu Cys His

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180	185	190	
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Gly Arg Gly Thr Cys Asn Tyr Tyr Ser Asn Ser Tyr Ser Phe Trp Leu			
195	200	205	
gct tca tta aac cca gaa aga atg ttc aga aag cct att cca tca act			672
Ala Ser Leu Asn Pro Glu Arg Met Phe Arg Lys Pro Ile Pro Ser Thr			
210	215	220	
gtg aaa gct ggg gaa tta gaa aaa ata ata agt cgc tgt cag gtg tgc			720
Val Lys Ala Gly Glu Leu Glu Lys Ile Ile Ser Arg Cys Gln Val Cys			
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 35 40 45  
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 50 55 60  
 Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys  
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 195 200 205  
 Ala Ser Leu Asn Pro Glu Arg Met Phe Arg Lys Pro Ile Pro Ser Thr  
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9/21

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<212> PRT  
<213> Artificial Sequence

<220>  
<223> ~~Canstatin (amino acids 1-244)~~ Deleted Sequence

<400> 19  
~~Pro Gly Leu Lys Gly Lys Arg Gly Asp Ser Gly Ser Pro Ala Thr Trp  
1 5 10 15  
Thr Thr Arg Gly Phe Val Phe Thr Arg His Ser Gln Thr Thr Ala Ile  
20 25 30  
Pro Ser Cys Pro Glu Gly Thr Val Pro Leu Tyr Ser Gly Phe Ser Phe  
35 40 45  
Leu Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln Asp Leu Gly Thr  
50 55 60  
Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys  
65 70 75 80  
Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr  
85 90 95  
Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr  
100 105 110  
Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr Val Cys Glu Gly~~

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115 120 125  
Pro Ala Ile Ala Ile Ala Val His Ser Gln Thr Thr Asp Ile Pro Pro  
130 135 140  
Cys Pro His Gly Trp Ile Ser Leu Trp Lys Gly Phe Ser Phe Ile Met  
145 150 155 160  
Phe Thr Ser Ala Gly Ser Glu Gly Thr Gly Gln Ala Leu Ala Ser Pro  
165 170 175  
Gly Ser Cys Leu Glu Glu Phe Arg Ala Ser Pro Phe Leu Glu Cys His  
180 185 190  
Gly Arg Gly Thr Cys Asn Tyr Tyr Ser Asn Ser Tyr Ser Phe Trp Leu  
195 200 205  
Ala Ser Leu Asn Pro Glu Arg Met Phe Arg Lys Pro Ile Pro Ser Thr  
210 215 220  
Val Lys Ala Gly Glu Leu Glu Lys Ile Ile Ser Arg Cys Gln Val Cys  
225 230 235 240  
~~Met Lys Lys Arg~~

<210> 20  
<211> 124  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Tumstatin 333 (amino acids ~~1-125~~ of SEQ ID NO:10)

<400> 20  
Gly Leu Lys Gly Lys Arg Gly Asp Ser Gly Ser Pro Ala Thr Trp Thr  
1 5 10 15  
Thr Arg Gly Phe Val Phe Thr Arg His Ser Gln Thr Thr Ala Ile Pro  
20 25 30  
Ser Cys Pro Glu Gly Thr Val Pro Leu Tyr Ser Gly Phe Ser Phe Leu  
35 40 45  
Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln Asp Leu Gly Thr Leu  
50 55 60  
Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys Asn  
65 70 75 80  
Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr Trp  
85 90 95  
Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr Gly  
100 105 110  
Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr Val  
115 120

<210> 21  
<211> ~~119~~ 120  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Tumstatin 334 (amino acids ~~125~~ 126-244 of SEQ ID NO:10)

<400> 21  
Cys Glu Gly Pro Ala Ile Ala Ile Ala Val His Ser Gln Thr Thr Asp  
1 5 10 15  
Ile Pro Pro Cys Pro His Gly Trp Ile Ser Leu Trp Lys Gly Phe Ser

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	20		25		30										
Phe	Ile	Met	Phe	Thr	Ser	Ala	Gly	Ser	Glu	Gly	Thr	Gly	Gln	Ala	Leu
	35						40					45			
Ala	Ser	Pro	Gly	Ser	Cys	Leu	Glu	Glu	Phe	Arg	Ala	Ser	Pro	Phe	Leu
	50					55					60				
Glu	Cys	His	Gly	Arg	Gly	Thr	Cys	Asn	Tyr	Tyr	Ser	Asn	Ser	Tyr	Ser
65					70					75				80	
Phe	Trp	Leu	Ala	Ser	Leu	Asn	Pro	Glu	Arg	Met	Phe	Arg	Lys	Pro	Ile
				85					90					95	
Pro	Ser	Thr	Val	Lys	Ala	Gly	Glu	Leu	Glu	Lys	Ile	Ile	Ser	Arg	Cys
			100					105					110		
Gln	Val	Cys	Met	Lys	Lys	Arg	His								
	115														

<210> 22

<211> 191

<212> PRT

<213> Artificial Sequence

<220>

<223> Tum-1 (Tumstatin N53) (amino acids 54-244 of SEQ ID NO:10)

<400> 22

<del>Asn</del>	Gln	Arg	Ala	His	Gly	Gln	Asp	Leu	Gly	Thr	Leu	Gly	Ser	Cys	Leu
1				5					10					15	
Gln	Arg	Phe	Thr	Thr	Met	Pro	Phe	Leu	Phe	Cys	Asn	Val	Asn	Asp	Val
			20					25					30		
Cys	Asn	Phe	Ala	Ser	Arg	Asn	Asp	Tyr	Ser	Tyr	Trp	Leu	Ser	Thr	Pro
	35					40					45				
Ala	Leu	Met	Pro	Met	Asn	Met	Ala	Pro	Ile	Thr	Gly	Arg	Ala	Leu	Glu
	50					55					60				
Pro	Tyr	Ile	Ser	Arg	Cys	Thr	Val	Cys	Glu	Gly	Pro	Ala	Ile	Ala	Ile
65					70					75				80	
Ala	Val	His	Ser	Gln	Thr	Thr	Asp	Ile	Pro	Pro	Cys	Pro	His	Gly	Trp
			85					90					95		
Ile	Ser	Leu	Trp	Lys	Gly	Phe	Ser	Phe	Ile	Met	Phe	Thr	Ser	Ala	Gly
		100						105					110		
Ser	Glu	Gly	Thr	Gly	Gln	Ala	Leu	Ala	Ser	Pro	Gly	Ser	Cys	Leu	Glu
	115						120					125			
Glu	Phe	Arg	Ala	Ser	Pro	Phe	Leu	Glu	Cys	His	Gly	Arg	Gly	Thr	Cys
	130					135					140				
Asn	Tyr	Tyr	Ser	Asn	Ser	Tyr	Ser	Phe	Trp	Leu	Ala	Ser	Leu	Asn	Pro
145					150					155				160	
Glu	Arg	Met	Phe	Arg	Lys	Pro	Ile	Pro	Ser	Thr	Val	Lys	Ala	Gly	Glu
			165						170					175	
Leu	Glu	Lys	Ile	Ile	Ser	Arg	Cys	Gln	Val	Cys	Met	Lys	Lys	Arg	His
		180						185					190		

<210> 23

<211> 132

<212> PRT

<213> Artificial Sequence

<220>

<223> Tum-2 (amino acids 1-132 of SEQ ID NO:10)



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<400> 23

~~Pro~~ Gly Leu Lys Gly Lys Arg Gly Asp Ser Gly Ser Pro Ala Thr Trp  
1 5 10 15  
Thr Thr Arg Gly Phe Val Phe Thr Arg His Ser Gln Thr Thr Ala Ile  
20 25 30  
Pro Ser Cys Pro Glu Gly Thr Val Pro Leu Tyr Ser Gly Phe Ser Phe  
35 40 45  
Leu Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln Asp Leu Gly Thr  
50 55 60  
Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys  
65 70 75 80  
Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr  
85 90 95  
Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr  
100 105 110  
Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr Val Cys Glu Gly  
115 120 125  
Pro Ala Ile Ala *Ile*  
130

<210> 24

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Tum-3 (amino acids 133-244 of SEQ ID NO:10)

<400> 24

~~Ile~~ Ala Val His Ser Gln Thr Thr Asp Ile Pro Pro Cys Pro His Gly  
1 5 10 15  
Trp Ile Ser Leu Trp Lys Gly Phe Ser Phe Ile Met Phe Thr Ser Ala  
20 25 30  
Gly Ser Glu Gly Thr Gly Gln Ala Leu Ala Ser Pro Gly Ser Cys Leu  
35 40 45  
Glu Glu Phe Arg Ala Ser Pro Phe Leu Glu Cys His Gly Arg Gly Thr  
50 55 60  
Cys Asn Tyr Tyr Ser Asn Ser Tyr Ser Phe Trp Leu Ala Ser Leu Asn  
65 70 75 80  
Pro Glu Arg Met Phe Arg Lys Pro Ile Pro Ser Thr Val Lys Ala Gly  
85 90 95  
Glu Leu Glu Lys Ile Ile Ser Arg Cys Gln Val Cys Met Lys Lys Arg *His*  
100 105 110

<210> 25

<211> 64

<212> PRT

<213> Artificial Sequence

<220>

<223> Tum-4 (amino acids 181-244 of SEQ ID NO:10)

<400> 25

~~Glu~~ Glu Phe Arg Ala Ser Pro Phe Leu Glu Cys His Gly Arg Gly Thr  
1 5 10 15  
Cys Asn Tyr Tyr Ser Asn Ser Tyr Ser Phe Trp Leu Ala Ser Leu Asn  
20 25 30

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Pro Glu Arg Met Phe Arg Lys Pro Ile Pro Ser Thr Val Lys Ala Gly  
35 40 45  
Glu Leu Glu Lys Ile Ile Ser Arg Cys Gln Val Cys Met Lys Lys Arg *His*  
50 55 60

<210> 26  
<211> 79  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Tum-5 (amino acids 54-132 of SEQ ID NO:10)

<400> 26  
~~Asn~~ Gln Arg Ala His Gly Gln Asp Leu Gly Thr Leu Gly Ser Cys Leu  
1 5 10 15  
Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys Asn Val Asn Asp Val  
20 25 30  
Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr Trp Leu Ser Thr Pro  
35 40 45  
Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr Gly Arg Ala Leu Glu  
50 55 60  
Pro Tyr Ile Ser Arg Cys Thr Val Cys Glu Gly Pro Ala Ile Ala *Ile*  
65 70 75

<210> 27  
<211> ~~20~~ *19*  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> T1 (amino acids 1-~~20~~ *19* of SEQ ID NO:10)

<400> 27  
~~Pro~~ Gly Leu Lys Gly Lys Arg Gly Asp Ser Gly Ser Pro Ala Thr Trp  
1 5 10 15  
Thr Thr Arg Gly  
20

<210> 28  
<211> 20  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> T2 (amino acids ~~54-73~~ *53-72* of SEQ ID NO:10)

<400> 28  
Asn Gln Arg Ala His Gly Gln Asp Leu Gly Thr Leu Gly Ser Cys Leu  
1 5 10 15  
Gln Arg Phe Thr  
20

<210> 29  
<211> 20

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<212> PRT

<213> Artificial Sequence

<220>

<223> T3 (amino acids ~~69-86~~<sup>68-87</sup> of SEQ ID NO:10)

<400> 29

Leu	Gln	Arg	Phe	Thr	Thr	Met	Pro	Phe	Leu	Phe	Cys	Asn	Val	Asn	Asp
1				5					10					15	
Val	Cys	Asn	Phe												
				20											

<210> 30

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> T4 (amino acids ~~84-103~~<sup>83-102</sup> of SEQ ID NO:10)

<400> 30

Asp	Val	Cys	Asn	Phe	Ala	Ser	Arg	Asn	Asp	Tyr	Ser	Tyr	Trp	Leu	Ser
1				5					10					15	
Thr	Pro	Ala	Leu												
				20											

<210> 31

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> T5 (amino acids ~~99-117~~<sup>98-116</sup> of SEQ ID NO:10)

<400> 31

Ser	Thr	Pro	Ala	Leu	Met	Pro	Met	Asn	Met	Ala	Pro	Ile	Thr	Gly	Arg
1				5					10					15	
Ala	Leu	Glu													

<210> 32

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> T6 (amino acids ~~114-132~~<sup>113-131</sup> of SEQ ID NO:10)

<400> 32

Arg	Ala	Leu	Glu	Pro	Tyr	Ile	Ser	Arg	Cys	Thr	Val	Cys	Glu	Gly	Pro
1				5					10					15	
Ala	Ile	Ala													

<210> 33

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<211> 88  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Tumstatin-45-132 (amino acids 45-132 of SEQ ID  
NO:10)

<400> 33  
~~Gly~~ Phe Ser Phe Leu Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln  
1 5 10 15  
Asp Leu Gly Thr Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro  
20 25 30  
Phe Leu Phe Cys Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn  
35 40 45  
Asp Tyr Ser Tyr Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met  
50 55 60  
Ala Pro Ile Thr Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr  
65 70 75 80  
Val Cys Glu Gly Pro Ala Ile Ala *Ile*  
85

<210> 34  
<211> 88  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Tumstatin-5-<sup>125</sup>126-C-A (amino acids 45-132 of SEQ ID  
NO:10; alanine has been substituted for the  
cysteine residue at position 126 of the  
full-length Tumstatin molecule) <sup>as</sup>

<400> 34  
~~Gly~~ Phe Ser Phe Leu Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln  
1 5 10 15  
Asp Leu Gly Thr Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro  
20 25 30  
Phe Leu Phe Cys Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn  
35 40 45  
Asp Tyr Ser Tyr Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met  
50 55 60  
Ala Pro Ile Thr Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr  
65 70 75 80  
Val Ala Glu Gly Pro Ala Ile Ala *Ile*  
85

<210> 35  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> synthetic blocking peptide

<400> 35  
Cys Asp Cys Arg Gly Asp Cys Phe Cys

1

5

<210> 36  
 <211> 5  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> synthetic blocking peptide

<400> 36  
 Cys Asn Gly Arg Cys  
 1 5

<210> 37  
 <211> 25  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> T7 (amino acids <sup>73 97</sup>~~74-98~~ of SEQ ID NO:10)

<400> 37  
 Thr Met Pro Phe Leu Phe Cys Asn Val Asn Asp Val Cys Asn Phe Ala  
 1 5 10 15  
 Ser Arg Asn Asp Tyr Ser Tyr Trp Leu  
 20 25

<210> 38  
 <211> 25  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> T7-mutant (amino acids <sup>73 97</sup>~~74-98~~ of SEQ ID NO:10;  
 methionine has been substituted for the leucine  
 residue at position ~~78~~ of the full-length  
 Tumstatin molecule, and isoleucine has been  
 substituted for valine at position ~~82~~, and  
 asparagine has been substituted for aspartic acid  
 at position ~~84~~  
<sup>83</sup>)

<400> 38  
 Thr Met Pro Phe Met Phe Cys Asn Ile Asn Asn Val Cys Asn Phe Ala  
 1 5 10 15  
 Ser Arg Asn Asp Tyr Ser Tyr Trp Leu  
 20 25

<210> 39  
 <211> 27  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> T8 (amino acids <sup>968 94</sup>~~99-95~~ of SEQ ID NO:10; lysine has

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been substituted for the leucine residue at  
position ~~68~~ of the full-length Tumstatin molecule)

<400> 39

Lys Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys Asn Val Asn Asp  
1 5 10 15  
Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser  
20 25

<210> 40

<211> 27

<212> PRT

<213> Artificial Sequence

<220>

<223> T8-3 (amino acids ~~68-95~~<sup>68 94</sup> of SEQ ID NO:10; lysine  
has been substituted for the leucine residue at  
position ~~68~~ of the full-length Tumstatin molecule,  
and serine has been substituted for the cysteine  
residues at positions ~~80~~<sup>79</sup> and ~~86~~<sup>85</sup>)

<400> 40

Lys Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Ser Asn Val Asn Asp  
1 5 10 15  
Val Ser Asn Phe Ala Ser Arg Asn Asp Tyr Ser  
20 25

<210> 41

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> TP3 (amino acids ~~77-95~~<sup>76 94</sup> of SEQ ID NO:10; lysine has  
been substituted for the phenylalanine residue at  
position ~~77~~ of the full-length Tumstatin molecule,  
and cysteine has been substituted for the aspartic  
acid at position ~~84~~<sup>83</sup>)

<400> 41

Lys Leu Phe Cys Asn Val Asn Cys Val Cys Asn Phe Ala Ser Arg Asn  
1 5 10 15  
Asp Tyr Ser

<210> 42

<211> 27

<212> PRT

<213> Artificial Sequence

<220>

<223> P2 (amino acids ~~68-95~~<sup>68 94</sup> of SEQ ID NO:10; lysine has  
been substituted for the leucine residue at  
position ~~68~~ of the full-length Tumstatin molecule,  
and aspartic acid has been substituted for the  
cysteine residues at positions ~~80~~<sup>79</sup> and ~~86~~<sup>85</sup>)

&lt;400&gt; 42

Lys	Gln	Arg	Phe	Thr	Thr	Met	Pro	Phe	Leu	Phe	Asp	Asn	Val	Asn	Asp
1				5					10					15	
Val	Asp	Asn	Phe	Ala	Ser	Arg	Asn	Asp	Tyr	Ser					
		20					25								

&lt;210&gt; 43

&lt;211&gt; 27

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Scrambled peptide SP1

&lt;400&gt; 43

Ala	Asn	Met	Ser	Arg	Asn	Val	Phe	Phe	Asp	Cys	Thr	Ser	Phe	Pro	Val
1				5					10					15	
Cys	Gln	Lys	Phe	Leu	Asn	Asp	Thr	Arg	Asn	Tyr					
		20					25								

&lt;210&gt; 44

&lt;211&gt; 27

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Scrambled peptide SP2

&lt;400&gt; 44

Thr	Phe	Asn	Cys	Val	Lys	Asn	Tyr	Gln	Arg	Leu	Asp	Phe	Thr	Ser	Arg
1				5					10					15	
Phe	Val	Met	Asp	Ser	Cys	Ala	Asn	Phe	Pro	Asn					
		20					25								

&lt;210&gt; 45

&lt;211&gt; 14

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Generic peptide

<223> X at position 1 is a <sup>any amino acid</sup> ~~hydrogen or a peptidyl chain~~  
~~of 1 to 17 amino acids~~

<223> X at position 2 is <sup>Phe Lys</sup> F or K

<223> X at position 5 is <sup>Cys Ser Asp</sup> C, S or D

<223> X at position 9 is <sup>Asp Cys</sup> D or C

<223> X at position 11 is <sup>Cys Ser Asp</sup> C, S or D

<223> X at position 14 is a <sup>any amino acid</sup> ~~hydrogen or a peptidyl chain~~  
~~of 1 to 12 amino acids~~

&lt;400&gt; 45

Xaa Xaa Leu Phe Xaa Asn Val Asn Xaa Val Xaa Asn Phe Xaa  
1 5 10

&lt;210&gt; 46

&lt;211&gt; 4

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Generic peptide

&lt;400&gt; 46

Thr Thr Met Pro  
1

&lt;210&gt; 47

&lt;211&gt; 5

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Generic peptide

&lt;400&gt; 47

Phe Thr Thr Met Pro  
1 5

&lt;210&gt; 48

&lt;211&gt; 6

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Generic peptide

&lt;400&gt; 48

Arg Phe Thr Thr Met Pro  
1 5

&lt;210&gt; 49

&lt;211&gt; 7

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Generic peptide

&lt;400&gt; 49

Gln Arg Phe Thr Thr Met Pro  
1 5

&lt;210&gt; 50

&lt;211&gt; 8



<212> PRT  
<213> Artificial Sequence

<220>  
<223> Generic peptide

<400> 50  
Leu Gln Arg Phe Thr Thr Met Pro  
1 5

<210> 51  
<211> 8  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Generic peptide

<400> 51  
Lys Gln Arg Phe Thr Thr Met Pro  
1 5

<210> 52  
<211> 4  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Generic peptide

<400> 52  
Ala Ser Arg Asn  
1

<210> 53  
<211> 5  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Generic peptide

<400> 53  
Ala Ser Arg Asn Asp  
1 5

<210> 54  
<211> 6  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Generic peptide

<400> 54

Ala Ser Arg Asn Asp Tyr  
1 5

<210> 55  
<211> 7  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Generic peptide

<400> 55  
Ala Ser Arg Asn Asp Tyr Ser  
1 5

<210> 56  
<211> 8  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Generic peptide

<400> 56  
Ala Ser Arg Asn Asp Tyr Ser Tyr  
1 5

<210> 57  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Generic peptide

<400> 57  
Ala Ser Arg Asn Asp Tyr Asp Tyr Trp  
1 5

<210> 58  
<211> 10  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Generic peptide

<400> 58  
Ala Ser Arg Asn Asp Tyr Ser Tyr Trp Leu  
1 5 10